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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,335	04/09/2004	Paul D. Wightman	58562US005	9992

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EXAMINER	
DESAI, RITA J	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
01/27/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

LegalUSDocketing@mmm.com
LegalDocketing@mmm.com

Office Action Summary	Application No.	Applicant(s)	
	10/821,335	WIGHTMAN ET AL.	
	Examiner	Art Unit	
	Rita J. Desai	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,10-12 and 14-51* is/are pending in the application.

4a) Of the above claim(s) *10 and 15-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,11,12 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1,3, 11, 12 and 14 are under examination.

Applicants have cancelled claims 2, 4-9, and 13.

Claims 10, and 15-51 have been withdrawn.

The rejection under § 102 and 103 Rejections over Gerster, Slade and Miller, and new rejection further in view of Langer.

Applicants argue that the compounds are covalently bonded to the support.

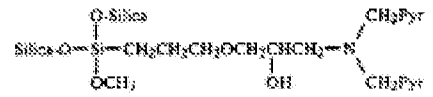
This may be so but 1) applicants claims are drawn to a a very broad scope and applicants just have a few examples.

2) it is well known that compounds can be covalently bonded to the solid support. Applicants own disclosure statement has reference which teach co-valently bonded compounds to solid support.

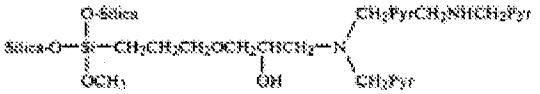
Applicants own priority admits that covalent bond exists between Avidin-biotin affinity-based technology has found wide applicability in numerous fields of biology and biotechnology since the pioneering work by Dr. Edward Bayer and Dr. Meier Wilchek in the 1970's. The affinity constant between avidin and biotin is remarkably high and is not significantly lessened when biotin is coupled to a wide variety of biomolecules. Numerous chemistries have been identified for coupling biomolecules to biotin with minimal or negligible loss in the activity or other desired characteristics of the biomolecule. A review of the biotin-avidin technology can be found in Applications of Avidin-Biotin Technology to Affinity-Based Separation, Bayer, et al., J. of Chromatography, 1990, pgs. 3-11.

Also see US 5078978 Byron Tarbet et al which teaches various Si bonded spacers covalently bonding solid supports an compound which form a complex with the metal. It is active which it is still attached to the solid support.

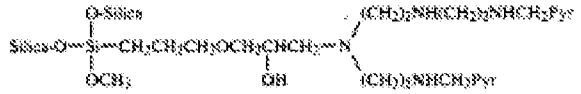
9. A method according to claim 8 wherein the pyridine containing ligand covalently bonded to a solid inorganic support has the formula:



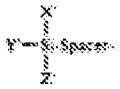
10. A method according to claim 8 wherein the pyridine containing ligand covalently bonded to a solid inorganic support has the formula:



11. A method according to claim 8 wherein the pyridine containing ligand covalently bonded to a solid inorganic support has the formula:



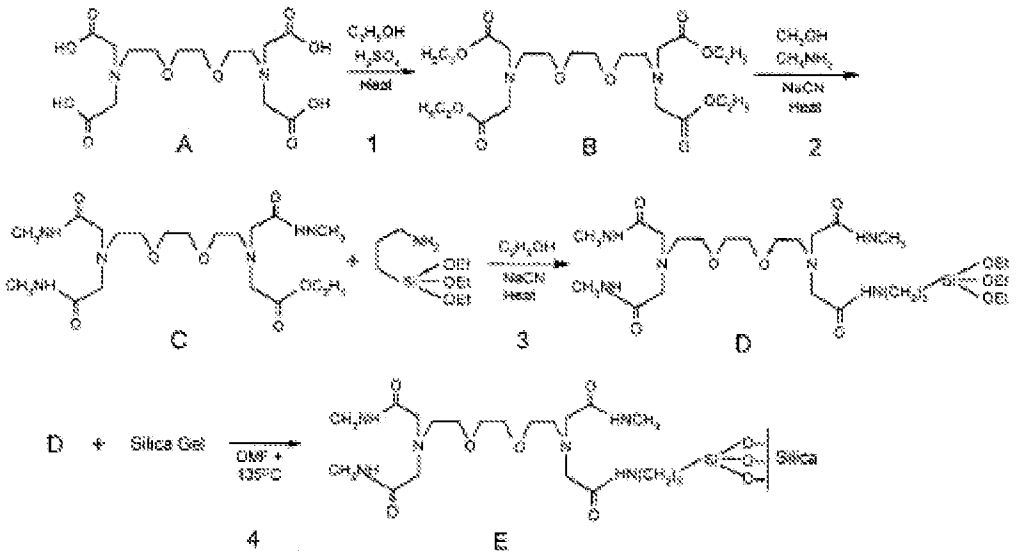
12. A method according to claim 3 wherein the



portion of the compound is a reaction product of O-solid hydrophilic support material with a silicon containing spacer grouping selected from the group consisting of dimethyl(triethoxysilylpropyl)malonate; 3-mercaptopropyltrimethoxysilane; 3-aminopropyltrimethoxysilane; N-[(3-trimethoxysilyl)propyl]ethylenediaminetriacetic acid; p-(chloromethyl)phenyltrimethoxysilane; vinyltriethoxysilane; 3-bromopropyltriethoxysilane; 3-glycidoxypropyltrimethoxysilane; and combinations thereof.

Also see WO 2001/023067 Breuning Ronald, teaches ligands bonded covalently to solid supports.

Example 1 - *Synthesis of dioxatetraamide [ethylene bis(oxyethylenenitrilo)tetraaceticacid (EGTAM)] attached to a silica support*



The whole document teaches about various covalent bonds to solid supports.

Thus it is well known that compounds can be covalently bonded to solid support and still remain active.

Langer further discloses this with respect to pharmaceuticals. Providing considerable motivation for one of skill in the art to make complexes of known drugs covalently bonded to solid support for delivery and activity at a desired location.

The rejection still stands.

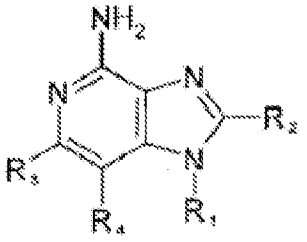
New Rejection

Double Patenting

Claims 1,3, 11, 12 and 14 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 of U.S. Patent No. 5078978. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to complexes of the same compounds with solid support.

1. (Currently amended) An immunostimulatory composition comprising:

an immune response modifier (IRM) portion of the formula:



and having IRM activity; and

a portion having antigenic activity that comprises:

an antigenic portion, or

a solid support to which an antigenic moiety is paired;

wherein the immune response modifier portion is covalently coupled to the portion having antigenic activity through R_1, R_2, R_3, or R_4;

wherein the immune response modifier portion comprises an imidazoquinoline amine; a tetrahydroimidazoquinoline amine; an imidazopyridine amine; an aryl ether-substituted imidazopyridine amine; a 1,2-bridged imidazoquinoline amine; a 6,7-fused cycloalkylimidazopyridine amine; an imidazonaphthyridine amine; a tetrahydroimidazonaphthyridine amine; an oxazoloquinoline amine; a thiazoloquinoline amine; an oxazolopyridine amine; a thiazolopyridine amine; an oxazolonaphthyridine amine; or a thiazolonaphthyridine amine; and

The previous rejection is being repeated here.

The rejection of he claims under 35 USC 102 /103 over Gerster , Slade and Miller et al has still stands as applicants have only shown limited compounds and bonds.

A new rejection under 35 USC 103 is being made over Gerster, Slade and Miller further in view of New Methods of Drug Delivery 1990. Robert Langer. 1990.

Gerster teaches and does disclose the polyethelene macro-molecules formulation. These could be bonded to the reactive groups on the IRM molecules. Could be H bonding too.

Applicants specifications on page 21, lines 19-21 clearly states that the IRM compound can be blended or mixed in. See below.

1RM can be released and formulated in that manner. That is. for example, the IRM can be simply dissolved or blended into a macromolecular support material (e,g,, as in a polymeric coating). Mixtures of the two types can also be used where desirable.

Applicants in their specification have not shown how the bonding takes place on the support. It just states it could be covalently bonded.

US 7,030,129 Miller et al.

The reference discloses the same IRM compound with the gel, paste and so on.

These are all the solid support, with the compounds forming an IRM-Support complex.

In view of the lack of disclosure and enablement of the specific bonding that forms the complex the reference clearly anticipates the invention.

Slade US 6894040 see column 5, lines 47 and 48 which discloses the 5% cream of imiquimod.

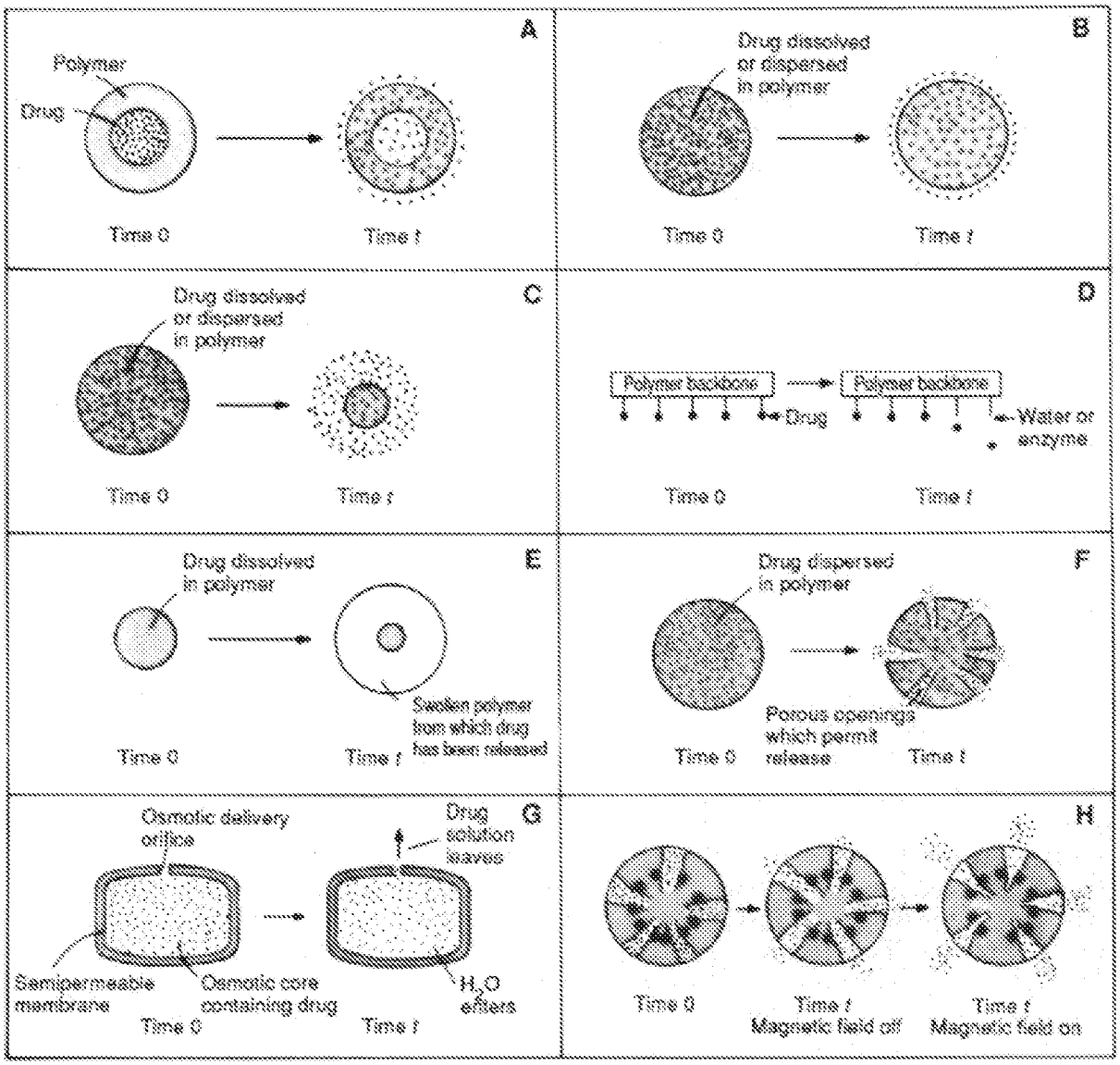
Langer et al at Column 2 teaches that drugs can be attached to macromolecules such as a polymer

research. Several experimental approaches have been developed, in which drugs are complexed to agents that enable them to cross this barrier (for example, by rendering the drug more lipophilic or coupling it to a molecule that has a specific transport mechanism) (*1*).

Drugs have also been attached to soluble macromolecules such as proteins, polysaccharides or synthetic polymers via degradable linkages. This process alters the drug's size and other properties, resulting in different pharmacokinetics and biodistribution. One example involves coupling the antitumor agent neocarzinostatin to styrene–maleic acid copolymers (*2*). When this complex was injected intra-arterially into patients with hepatocellular carcinoma, decreases in α-fetoprotein levels and tumor size were observed. In animals, antitumor agents such as doxorubicin coupled to *N*-(2-hydroxypropyl) methacrylamide copolymers showed radically altered pharmacokinetics, resulting in reduced toxicity. The half-life of

Polymers, such as polyethylene glycol (PEG), can be attached to drugs to either lengthen their lifetime or alter their immunogenicity. The polymers physically prevent cells and enzymes from attacking the drug. PEG-uricase reduced serum urate levels in patients with hyperuricemia and gout; PEG-asparaginase has been used for patients with leukemia, and PEG–adenosine deaminase has been used for patients with a severe combined immunodeficiency (*6*). Drug longevity and immunogenicity may also be affected by biological approaches, including protein engineering and altering glycosylation patterns

Controlled release systems provide advantages over conventional drug therapies. For example, after ingestion or injection of standard dosage forms, the blood level of the drug rises, peaks, and then declines. Since each drug has a therapeutic range above which it is toxic and below which it is ineffective, oscillating drug levels may cause alternating periods of ineffectiveness and toxicity. Although sustained release preparations attenuate the peaks and valleys, they do not eliminate them. In contrast, a controlled release preparation maintains the drug in the desired therapeutic range by a single administration. Other potential advantages of controlled release systems include (i) localized delivery of the drug to a particular body compartment, thereby lowering the systemic drug level; (ii) preservation of medications that are rapidly destroyed by the body (this is particularly important for biologically sensitive molecules such as proteins); (iii) reduced need for follow-up care; (iv) increased comfort; and (v) improved compliance.



The whole reference talks about methods for delivering drugs making a complex of a drug with a macromolecule.

See figure D which shows the drug attached to a macromolecule.

On page 1 line 30 of the specifications applicants clearly state that he need for a better form of delivery of these drugs is required.

Thus the prior art teaches making complex es of the drug with macromolecules for improving the delivery. Thus one of skill in the art of drug delivery would have been motivated to make the macromolecular complexes of the IRM compounds to enhance the delivery of the compound specific sites.

KSR International. v Teleflex 2007 which gives a number of rationales for obviousness rejections.

> When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, 35 U.S.C. 103 bars its patentability.

> "A person of ordinary skill in the art is also a person of ordinary creativity, not an automaton." [31] "[I]n many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle." [32]

> Office personnel may also take into account "the inferences and creative steps that a person of ordinary skill in the art would employ." [33]

The case gives numerous rationales as given below.

Rationales

(A) Combining prior art elements according to known methods to yield predictable results;

(B) Simple substitution of one known element for another to obtain predictable results;

(C) Use of known technique to improve similar devices (methods, or products) in the same way;

(D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results;

(E) "Obvious to try"—choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;

(F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations would have been predictable to one of ordinary skill in the art;

(G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

In this case the problem to be solved is to be able to deliver the drug at the various cites.

The Langer reference teaches making complexes of the drug and a macromolecule. And thus would motivate one of skill in the art to try to make the complexes, especially since applicants claims have a compounds encompassing a very large core and just a handful of complexes made.

The rejection of the claims under 35 USC 112 first para on claim 1-5 still stands.

Even though applicants have amended claim 1 to include specific cores , these include several cores and applicants have exemplified only the pyridine imidazole and the quinoline imidazole. The cores included encompasses numerous compounds. Applicants have incorporated by reference in the specifications several patents. The limited examples shown and disclosed are drawn to specific compounds and specific linkers.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rita J. Desai/

Primary Examiner, Art Unit 1625

RD.
January 18, 2009